

**The part played by an "accessory factor" in the production of experimental rickets.** By EDWARD MELLANBY.

In these experiments puppies of about two months old were fed on diets which were found to produce rickets in the course of 3-4 months. Two such diets were used:

- (1) Milk, rice, oatmeal and sodium chloride,
- (2) Milk and bread.

Salt is essential for life in the case of the first diet. The milk must be limited to less than 200 c.c. each day. If it is much increased no rickets develop.

In the case of other puppies, different classes of foodstuffs were added to the ricketty diet and the development or non-development of the disease investigated. The results were of such a nature that if rickets did not develop it could be assumed that it contained some anti-rachitic factor.

The following lists briefly indicate some of the results obtained:

Substances preventing rickets	Substances not preventing rickets
(1) Meat.	(1) Protein of meat.
(2) Watery extract of meat free from protein.	(2) Casein.
(3) Malt extract.	(3) Linseed oil.
(4) Commercial yeast extract.	(4) 10 grams of yeast a day.
(5) 500 c.c. of milk each day.	
(6) Butter.	
(7) Margarines.	
(8) Cod liver oil.	

An examination of these tables shows that fats, proteins and carbohydrates are not causative factors. On the other hand it seems clear that rickets is a deficiency disease of the type of scurvy and beri-beri. Similarly the anti-rachitic accessory factor has characters related to the growth accessory factor, although it is not identical with the latter, since rickets is rather an abnormality of growth and is most prominently shown in quickly growing animals.

Exercise may be an additional factor in the development of rickets but is not primary. Several dogs were kept on a mixed diet containing meat and confined without exercise for some months. They did not develop rickets. On the other hand puppies on a ricket's diet, however

much freedom they are allowed, become lethargic in their movements some time before the legs bend. There is a physical flabbiness about them that one associates with rachitic children. When the condition is really developed no real exercise is possible owing to the physical disabilities.

To sum up:

(1) Rickets is a condition primarily due to the lack of an accessory factor in the diet.

(2) This accessory factor is found in (i) Extractives especially meat, (ii) Fats especially butter but not in linseed oil.

(3) Lack of exercise may play some part but not a primary part in the development.

The volume discharged by the siphon depends, in part, on the orientation of the latter. By rotating *A* clock-wise (about a horizontal axis perpendicular to the plane of the paper) the bend of *C* is raised and the capacity of the siphon is increased and vice versa. By this means the discharge of a siphon giving 8–12 c.c., when *A* is vertical, may be varied by  $\pm$  2–4 c.c. and adjusted, readily, to give any desired volume within these limits. The discharge of the siphon must, obviously, be adjusted and measured with the tambour connected to *B*.

## REFERENCE

- (1) This *Journal*, 50. 1915–16. These *Proceedings* p. xxxiii.

**A further demonstration of the part played by accessory food factors in the ætiology of rickets.** By EDWARD MELLANBY.

In a previous demonstration to this Society of puppies showing the part played by diet in producing and preventing Rickets, it was seen that, using a standard rachitic diet of bread and milk (175 c.c.), the disease was prevented by butter, cod liver oil and most other fats tested, increased milk (500 c.c.), meat and meat extracts, but was not prevented by yeast, linseed oil and the proteins of milk and meat. On the basis of these results, an attempt was made to improve the standard rachitic diet in order to produce a more rapid development of the disease and to render it less easy to prevent. In the dogs demonstrated today, the standard diet has been separated milk (175–350 c.c.), 70 per cent. wheaten bread *ad lib.*, linseed oil 5–10 c.c., yeast 5–10 grams, orange or lemon juice 3 c.c., sodium chloride 2 grams. This diet will produce a rapid development of rickets, easily recognisable by X-ray photograph within 6 weeks of beginning the diet. In the puppies exhibited it will be seen that

(1) lean meat (10 grams a day) only delays but does not prevent rickets and that the extent of the delay depends on the initial weight and rate of growth of the animal. The greater the rate of growth, the less is the effect of meat.

(2) increasing the separated milk to 350–400 c.c. per diem does not prevent rickets. This excludes the possibility that the calcium intake is deficient.

(3) 10 grams of butter or cod liver oil, even on the above diet, completely prevents rickets.

(4) 10 grams of cotton seed oil, olive oil or babassu oil per diem does not prevent rickets when substituted for linseed oil.

All vegetable oils are not equally ineffective in preventing rickets. Linseed oil is the worst of those tested, then in order of increasing merit, tentatively suggested, babassu, cotton-seed, peanut (*arachis*) and olive. A hydrogenated fat tested was similar to linseed oil. Suet and lard appear (experiment not completed) to prevent rickets if 10 grams of meat per diem is also eaten. A small amount of meat helps an otherwise ineffective fat.

The above facts are for the most part in keeping with the idea that rickets is a disease primarily due to a deficiency of Fat-soluble A. Animal fats are the best preventatives.

It is difficult, however, to fit the inhibitory action of lean meat, meat and malt extracts into this theory.

Other facts brought out in this work are:

(1) the more rapidly growing the dog, the more anti-rachitic factor is required to keep the growth straight.

(2) while not yet able to deny the necessity of Fat-soluble A being present in a diet to ensure growth, it is the case that many of my more rapidly growing puppies have had the least Fat-soluble A. This accessory factor seems to be more essential for ensuring normal growth as opposed to abnormal growth and keeping the tissues in good working order.

(3) taking this work in conjunction with my wife's research on factors affecting the formation of teeth<sup>1</sup>, it appears that those substances containing and associated with Fat-soluble A are particularly concerned in the calcification processes of bones and teeth. Further, the close relationship between rickets and defective teeth (both as regards enamel formation and arrangement in the jaws) is placed on an experimental basis.

**A note in reference to segmental distribution of blood-vessels in the upper limb.** By JUDAH LEON JONA.

It has occurred to me that possibly the following notes would be of interest. On 8. v. 1918 I stumbled, fell on my right elbow with arm out-stretched, and dislocated my right shoulder, the head of the humerus occupying a subclavicular position. It was reduced under chloroform within an hour of the occurrence. The X-ray photograph showed a little tearing up of the periosteum off the lower part of the neck of the humerus. The arm was put at rest—absolutely immobilised for 48 hours and then put up in a sling support which kept the shoulder joint and humerus

<sup>1</sup> The effect of diet on teeth formation. May Mellanby, *Lancet*, December 7, 1918.